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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,362	06/22/2001	Patrick J. Muraca	5568/1012	8909

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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,362	MURACA, PATRICK J.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-15 and 35-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-15 and 35-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 9, 2004 has been entered.

Status of the Application

2. Claims 1-4, 7-15 and 35-65 are pending and are rejected herein. This action is made NON-FINAL.

Priority

3. Applicant's claim to priority of US Provisional Applications 60/213,321, filed on June 22, 2000; 60/234,493, filed on September 22, 2000; and 60/236,649, filed on September 29, 2000, has been acknowledged. However, the instant claims have not been granted priority to any of these provisional applications. Specifically, the instant claims now recite, "a tissue microarray comprising a cooling chamber" (Claim 1), and "a tissue microarrayer comprising a cooling chamber" (Claim 12). The provisional applications do not provide support for the limitations reciting, "a tissue microarray comprising a cooling chamber", and "a tissue microarrayer

comprising a cooling chamber". Accordingly, the effective filing date of the instant claims is the filing date of the instant non-provisional application, June 22, 2001.

Specification

4. The disclosure is objected to because on page 22, line 23, the specification recites, "U.S. Patent Application Serial No. 09/779,753", which could be amended to include, "now U.S. Patent No. 6,534,307".

Appropriate correction is required.

Claim Rejections - 35 USC § 112 - New Matter

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1-4 and 7-11 are drawn to a method of "preparing a microarray of frozen tissue...providing a tissue microarray comprising a cooling chamber" (see Claim 1). However, there is no support in the specification for a "tissue microarray comprising a cooling chamber". Starting on page 10 of Applicant's response, filed on September 10, 2003, Applicant assert

support for the instant claims can be found on pages 22-23, 26 and 28. These pages refer to a device for generating microarray blocks, referred to as a "microarrayer". (See page 22, lines 16-24). Specifically, Applicant incorporates by reference the "microarrayer" which is described in U.S. Patent Application Serial No. 09/779,753 (now U.S. Patent No. 6,534,307). Accordingly, while there is support for generating a microarray block using a "microarrayer" comprising a cooling chamber, there is no support for a "tissue microarray" comprising a cooling chamber.

Claim Rejections - 35 USC § 112 - Indefiniteness

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-4, 7-15 and 35-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-4, 7-11 and 35-65 are indefinite because it is not clear that a "tissue microarray" can comprise a cooling chamber. The specification refers to a cooling chamber that is used in conjunction with a device that forms microarray blocks, but not that the microarray itself comprises a "cooling chamber".

B) Claims 12-15 are indefinite because it is not clear as to how the "tissue microarrayer" is being used in the method or exactly what is encompassed by the recitation of "tissue microarrayer". For example, step c) is drawn to "providing a tissue microarrayer comprising a cooling chamber", however the remainder of the claim makes no mention of the microarrayer or how it is used to create a microarray block. Accordingly, it is not clear as to how step c) is

involved with or contributes to the accomplishment of the claimed method. Furthermore, the recitation of "tissue microarrayer" is not specifically defined in the specification. It is noted that the specification refers to a "tissue microarrayer" by incorporation of Applicant's U.S. Patent Application Serial No. 09/779,753 (now U.S. Patent No. 6,534,307); however, this patent does not define this recitation either. More specifically, it is not clear the skilled artisan would know exactly what is encompassed (structurally and functionally) by a tissue microarrayer comprising a cooling chamber, absent any clear structural and functional limitations of the "tissue microarrayer".

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-4, 7-15 and 35-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leighton (USPN 6,103,518), in view of Irving et al. (J of Clin. Path. (1996) 49: 258-259), and in further view of Gordon, A. (USPN 5,533,342).

Leighton teaches a method for constructing tissue microarrays (also referred to as "tissue Chips") comprising,

"taking samples from a series of donor tissues, one at a time, using a hollow, preferably needlelike, donor punch and placing each sample sequentially in a recipient of complementary shape in a recipient material by a recipient punch, thereby forming an array of tissues in the recipient block. Each punch comprises a punch tube and an associated stylet guided within the diameter approximating that of the donor punch inner diameter, and is dimensioned for sliding within the punch tube. The process of forming a hole in a recipient material such as paraffin,

taking a sample of tissue from a donor specimen, and planting this sample in the hole in the recipient material, is repeated until a tissue array is formed comprising hundreds of tissue samples arranged in assigned locations in the recipient material. (col. 7).

"Once the desired number of tissue samples have been transplanted from the donor block(s) to the recipient block, the "tissue chips" can be formed by slicing the tissue array block into hundreds of consecutive thin sections of, e.g., 5 micrometers in thickness, by traditional means (i.e., microtomes such as Model Cut .sub. 4055.TM. by Olympus Corp. of Tokyo, Japan, etc.; see, e.g., U.S. Pat. Nos. 664,118; 2,292,973; 2,680,992; 3,420,130; 3,440,913; 3,496,819; 3,799,029; and 3,975,977) to create multiple nearly identical sections, with each of the donor cores then being represented as minuscule dots on an ordinary glass microscope slide. Analyses that may be performed on the donor specimens include immunological analysis, nucleic acid hybridization, and clinicopathological characterization of the specimen." (col. 13).

Leighton also teaches:

"The sample punched from the donor tissue sample is preferably cylindrical, about 1-8 mm in length, with a diameter of from about 0.4 to 4.0 mm, preferably about 0.3-2.0 mm. The recipient punch is slightly smaller than the donor punch and is used to create a hole in a recipient block, typically made of paraffin or other embedding medium." (col. 7).

Leighton also teaches that the methods can be automated and information for each donor sample in the recipient block is stored in a database (col. 7). Leighton also teaches that this array can be used for many types of samples, including diseased samples (col. 1-4). It is also noted, that with respect to claims 54-65 (claims drawn to contacting the microarray with a molecular probe), Leighton teaches that the array made in his methods can be used in nucleic acid hybridization, which would inherent use a molecular probe for detection (e.g., determining which sublocation react).

Leighton teaches that the tissue samples are embedded in a block of paraffin or other embedding material. Leighton does not specifically teach the use of frozen embedding material.

However, Irving teaches that storing pathological tissue or cell specimens in OCT embedding material (i.e., a frozen embedding material) "permits retrospective analysis of RNA from small amounts of stored pathological samples" (see abstract). In other words, Irving

teaches that embedding samples in OCT embedding material produces high quality RNA (i.e., RNA is not likely to get degraded in OCT, as it would in paraffin embedding material) (pg. 258).

Gordon teaches that when tissue samples are stored in freezing embedding material, it is advantageous to perform the preparation of a tissue block in a cooling chamber (e.g., a cryostat or freezing station) (see abstract, and cols. 1, lines 5-12 and 25-62; col. 3, lines 39-67; col. 3, lines 23-67; cols. 5, 7 and 9). Specifically, Gordon teaches,

> In a typical prior art procedure for freezing, cutting and preparing a surgical specimen for microscopic examination, the tissue sample is brought into the laboratory for diagnosis while the patient is still on the operating table. Thus, as can be easily appreciated, it is essential to freeze, cut, and diagnose the section of tissue specimen as quickly as possible. Any unnecessary delays can be life threatening. In order to minimize the time required to perform the critical steps of freezing, cutting and diagnosis of a tissue section, an embedding medium (e.g., an aqueous solution, a viscous aqueous solution, or a viscous aqueous gel) is dispensed onto a specimen holder or block holder which is usually in the form of a small metal block. The specimen is either placed on top of or submerged into the embedding medium, and then is frozen by any number of means. In most prior art cryostats, the tissue specimen holder is placed on a cold shelf (the freezing shelf) where the medium and tissue specimen are frozen...As can be appreciated, regardless of the freezing technique incorporated, it is generally desirable that the tissue be frozen at the lowest possible temperature (and therefore as quickly as possible) since more rapid freezing results in the formation of smaller ice crystals, and therefore, less damage to the tissue morphology. Also, since the tissue itself is a poor thermal conductor, the best frozen tissue to examine is the tissue at the surface closest to the cooling source. The tissue layers which are further from the surface freeze more slowly (due to the low thermal conductivity of tissue) and therefore have larger ice crystals and poorer quality tissue morphology.

(col. 1, lines 39-62). Accordingly, Gordon teaches the use of a cooling chamber for preparation of tissue blocks is advantageous for maintaining the integrity of the tissue sample and can minimize the time required to perform the critical steps of freezing, cutting and diagnosis of a tissue section.

In view of the teachings of Irving and Gordon, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of

Leighton so as to have embedded tissue and/or cell samples in OCT embedding material in a cooling chamber, in order to have achieved the benefit of providing a higher quality RNA, which would help obtain better results when analyzing the tissue and/or cell samples in subsequent molecular analysis (such as expression analysis). Furthermore, one skilled in the art would have been motivated to prepare tissue microarrays within a cooling chamber, in order to have maintained the integrity of the tissue sample and minimized the time required to perform the critical steps of freezing, cutting and diagnosis of a tissue section.

11. Claims 1-4, 7-15 and 35-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leighton (USPN 6,103,518), in view of Goldsworthy et al. (Mol. Carcinog (1999) 25(2): 86-91), and in further view of Gordon, A. (USPN 5,533,342).

The teachings of Leighton are presented above. Specifically, Leighton teaches the preparation of a tissue microarray, wherein the tissue samples are embedded in a block of paraffin or other embedding material. Leighton does not specifically teach the use of frozen embedding material.

However, Goldsworthy teaches that "frozen tissues yielded more RT-PCR product than did paraffin-embedded tissues" when analyzing liver tissue expression (see abstract and pg. 87). Goldsworthy concludes that one of the reasons for this that, "the longer exposure of the fresh tissues to the fixative before embedding in paraffin may have resulted in RNA degradation from endogenous RNases, resulting in lower amounts of amplifiable RNA" (pg. 90, second column). Goldsworthy's results, like others in the art, further support the idea that better results of amplification of RNA from tissues are obtained by using methods other than paraffin blocks (pg. 90, second column).

The teachings of Gordon are presented above. Specifically, Gordon teaches the use of a cooling chamber for preparation of tissue blocks is advantageous for maintaining the integrity of the tissue sample and can minimize the time required to perform the critical steps of freezing, cutting and diagnosis of a tissue section.

In view of the teachings of Goldsworthy and Gordon, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Leighton so as to have embedded tissue and/or cell samples in a frozen embedding material in a cooling chamber, in order to have achieved the benefit of providing a higher quality RNA, which would help obtain better results when analyzing the tissue and/or cell samples in subsequent molecular analysis (such as expression analysis). Furthermore, one skilled in the art would have been motivated to prepare tissue microarrays within a cooling chamber, in order to have maintained the integrity of the tissue sample and minimized the time required to perform the critical steps of freezing, cutting and diagnosis of a tissue section.

Response to Applicant's Arguments

Applicant's arguments are drawn to the previous 103 rejections of Leighton in view of Irving (or Goldsworthy), and rest on the argument that these references do not teach the newly added limitation of a microarrayer comprising a cooling chamber. Applicant's arguments have been considered, but are not persuasive in light of the new 103 rejections of Leighton in view of Irving (or Goldsworthy) and Gordon, as presented above.

12. Claims 1-4, 7-15 and 35-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi et al. (Pub. No. US 2002/0132246), in view of Irving et al. (J of Clin. Path. (1996) 49: 258-259), and in further view of Gordon, A. (USPN 5,533,342).

Kallioniemi teaches a method for making a tissue microarray:

"In a specific example, core tissue biopsies having a diameter of 0.6 mm and a height of 3-4 mm, were taken from selected representative regions of individual "donor" paraffin-embedded tumor blocks and precisely arrayed into a new "recipient" paraffin block (20 mm.times.45 mm). H&E-stained sections were positioned above the donor blocks and used to guide sampling from morphologically representative sites in the tumors. Although the diameter of the biopsy punch can be varied, 0.6 mm cylinders have been found to be suitable because they are large enough to evaluate histological patterns in each element of the tumor array, yet are sufficiently small to cause only minimal damage to the original donor tissue blocks, and to isolate reasonably homogenous tissue blocks.

With the adhesive film in place, a 4-8 .mu.m section of the recipient block is cut transverse to the longitudinal axis of the tissue cylinders (FIG. 5) to produce a thin microarray section 76 (containing tissue specimen cylinder sections in the form of disks) that is transferred to a conventional specimen slide 78. The microarray section 76 is adhered to slide 78, for example by adhesive on the slide. The film 74 is then peeled away from the underlying microarray member 76 to expose it for processing. A darkened edge 80 of slide 78 is suitable for labeling or handling the slide." (pg. 5, Figs. 1-10 and 15-17).

Kallioniemi teaches that the samples can be that the methods can be automated and information for each donor sample in the recipient block is stored in a database (pg. 5, for example). Additionally, Kallioniemi teaches microarray can be used for many types of samples, including diseased samples (pgs. 1-4, Ex. 1-14). Kallioniemi also teaches methods including contacting the microarray with a molecular probe (pgs. 1-4, for example).

Kallioniemi does not specifically teach the use of frozen embedding material.

However, Irving teaches that storing pathological tissue or cell specimens in OCT embedding material (i.e., a frozen embedding material) "permits retrospective analysis of RNA from small amounts of stored pathological samples" (see abstract). In other words, Irving teaches that embedding samples in OCT embedding material produces high quality RNA (i.e., RNA is not likely to get degraded in OCT, as it would in paraffin embedding material) (pg. 258).

The teachings of Gordon are presented above. Specifically, Gordon teaches the use of a cooling chamber for preparation of tissue blocks is advantageous for maintaining the integrity of the tissue sample and can minimize the time required to perform the critical steps of freezing, cutting and diagnosis of a tissue section.

In view of the teachings of Irving and Gordon, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Kallioniemi so as to have embedded tissue and/or cell samples in OCT embedding material in a cooling chamber, in order to have achieved the benefit of providing a higher quality RNA, which would help obtain better results when analyzing the tissue and/or cell samples in subsequent molecular analysis (such as expression analysis). Furthermore, one skilled in the art would have been motivated to prepare tissue microarrays within a cooling chamber, in order to have maintained the integrity of the tissue sample and minimized the time required to perform the critical steps of freezing, cutting and diagnosis of a tissue section.

13. Claims 1-4, 7-15 and 35-65 rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi et al. (Pub. No. US 2002/0132246), in view of Goldsworthy et al. (Mol. Carcinog (1999) 25(2): 86-91).

The teachings of Kallioniemi are presented above. Specifically, Kallioniemi teaches the preparation of a tissue microarray, wherein the tissue samples are embedded in a block of paraffin. Kallioniemi does not specifically teach the use of frozen embedding material.

However, Goldsworthy teaches that "frozen tissues yielded more RT-PCR product than did paraffin-embedded tissues" when analyzing liver tissue expression (see abstract and pg. 87). Goldsworthy concludes that one of the reasons for this that, "the longer exposure of the fresh

tissues to the fixative before embedding in paraffin may have resulted in RNA degradation from endogenous RNases, resulting in lower amounts of amplifiable RNA" (pg. 90, second column). Goldsworthy results, like others in the art, further support the idea that better results of amplification of RNA from tissues are obtained by using methods other than paraffin blocks (pg. 90, second column).

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Applicant's arguments are drawn to the previous 103 rejections of Kallioniemi in view of Irving (or Goldsworthy), and rest on the argument that these references do not teach the newly added limitation of a microarrayer comprising a cooling chamber. Applicant's arguments have

been considered, but are not persuasive in light of the new 103 rejections of Kallioniemi in view of Irving (or Goldsworthy) and Gordon, as presented above.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-15 and 35-65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 and 19-24 of U.S. Patent No. 6,582,967. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '967 are a species of the instant claims, and therefore, render the instant claims obvious.

For example, Claim 1 of the instant claim recites,

A method for preparing a microarray of frozen tissue and/or cell samples comprising the steps of:

(a) obtaining a donor sample from a donor block comprising a tissue or cell sample embedded in frozen embedding material:

(b) providing a recipient block comprising a frozen embedding material;

(c) providing a tissue microarray comprising a cooling chamber;

(d) generating a hole in said recipient block sized to receive said donor sample:

(e) filing said hole in said recipient block with said donor sample;

(f) repeating steps (a)-(e) to create a microarray block comprising a plurality of donor tissue and/or cell samples embedded in a block of frozen embedding material, each of said donor sample having a known location in said block;

(g) sectioning said microarray block to generate a section comprising portions of said plurality of donor samples, each portion of each donor sample at a different sublocation in the section at coordinates corresponding to coordinates of the donor sample in the microarray block from which each portion was obtained; and

(h) placing said section on a substrate such that said portions at different sublocations are stably associated with said substrate, thereby generating said microarray.

The relevant Claims of '967 recite,

> 1. A method for forming a microarray block, comprising: (a) providing a donor block comprising a frozen tissue sample wherein said donor block is placed in a cooling chamber for receiving said frozen tissue sample and for maintaining said frozen tissue sample in a frozen condition; (b) obtaining a core of frozen tissue from said donor block; (c) providing a recipient block comprising a frozen embedding matrix; (d) generating a hole in said recipient block for receiving said core of frozen tissue; and (e) placing said core of tissue in said hole in said recipient block.
>
> 2. The method according to claim 1, comprising repeating steps (a) through (d) multiple times.
>
> 3. The method according to claim 1, further comprising the step of placing said donor and recipient blocks in said cooling chamber.
>
> 4. The method according to claim 1, wherein said step of obtaining said core of frozen tissue comprises coring said frozen tissue with a coring needle.

5. The method according to claim 1, further comprising: obtaining a section of tissue from said donor block and identifying coordinates of a tissue sample of interest in said section; and obtaining said core of frozen tissue from a portion of the donor block comprising identical coordinates.

6. The method according to claim 5, wherein said identifying is performed using a microscope.

7. The method according to claim 5, wherein said tissue sample of interest comprises abnormally proliferating cells.

8. The method according to claim 5, wherein said step of identifying comprises reacting said section with a molecular probe and identifying coordinates on said section where said tissue reacts with said molecular probe.

9. The method according to claim 5, wherein said step of identifying comprises reacting said section with a molecular probe and identifying coordinates on said section wherein said tissue does not react with said molecular probe.

10. The method according to claim 8 or 9, wherein said molecular probe is an antibody or a nucleic acid.

11. The method of claim 5, wherein said step of obtaining said core from said donor block and generating said hole in said recipient block are performed simultaneously.

12. The method of claim 5, wherein said step of obtaining said core from said donor block and creating said hole in said recipient block are performed sequentially.

13. A method for forming a microarray block comprising: (a) providing a donor block comprising a frozen tissue sample wherein said donor block is placed in a cooling chamber for receiving said frozen tissue sample and for maintaining said frozen tissue sample in a frozen condition; (b) providing a recipient block comprising a frozen embedding matrix comprising at least one hole for receiving a core of frozen tissue; (c) obtaining a core of frozen tissue from said donor block; and (d) placing said core of tissue in said hole in said recipient block.

14. A method for forming a microarray block comprising: a) providing a device comprising: a fixed horizontal surface; a cooling chamber for receiving at least one frozen material and for maintaining said frozen material in a frozen condition; said cooling chamber moveable in an x- and y-direction relative to said fixed horizontal

surface; at least one coring needle, said coring needle comprising a cutting surface and a lumen for receiving a core of frozen material cut by said cutting surface; and at least one coring needle positioning element, for positioning said at least one coring needle over said frozen material for cutting said frozen material; b) placing a frozen tissue sample in said cooling chamber; c) positioning said at least one coring needle over said tissue sample; d) obtaining a core of tissue sample from said frozen tissue sample using said at least one coring needle; e) placing a block of frozen embedding medium in said cooling chamber; f) positioning said at least one coring needle over said block of frozen embedding medium; g) coring a hole in said block of frozen embedding medium; and h) placing said core of tissue sample in said hole.

15. The method according to claim 14, wherein said step of obtaining said core of tissue sample is performed using a first coring needle and said step of coring said hole in said block of frozen embedding medium is performed using a second coring needle.

19. The method according to any of claims 5, 13, and 14, further comprising the step of sectioning said microarray block thereby obtaining a section comprising a plurality of sectioned tissue samples.

20. The method according to claim 19, further comprising the step of placing said section comprising said plurality of tissue samples on a substrate.

21. The method according to claim 20, wherein said substrate is a glass slide.

22. The method according to any of claims 5, 13, or 14, wherein information regarding the coordinates of a hole into which a tissue sample is placed and the identity of a tissue sample at that hole is recorded and stored in a database.

23. The method according to claim 22, wherein said database comprises patient information relating to the source of a tissue sample placed in said hole.

24. The method according to claim 23, wherein said information is one or more of: data relating to tissue type, developmental stage, disease presence, disease progression, patient medical history, family medical history, and expression of one or more biomolecules in the tissue sample.

Accordingly, because the claims of the '967 represent specific embodiments (i.e., a species) of the genus claims of the instant invention, the claims of '967 are obvious over the

claims of the instant invention. It is noted that the instant claims are drawn to a "microarrayer comprising a cooling chamber"; '967 teaches the donor block is placed in a microarrayer comprising cooling chamber with specific structural limitations (see, for example Claim 14 of '967).

Conclusion

15. No claims are allowable.

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kononen et al. (USPN 6,699,710)

Correspondence

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If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

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